PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 12456910/E	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/AU2004/000749	International filing date *(day/month/year)* 4 June 2004	Priority date *(day/month/year)* 4 June 2003

International Patent Classification (IPC) or national classification and IPC

Int. Cl.[7] C12Q 1/68 C12N 15/00 A01K 67/00

Applicant

THE WALTER AND ELIZA HALL INSTITUTE OF MEDICAL RESEARCH et al

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *(sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or table related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of the report
4 April 2005	22 April 2005
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **LEXIE PRESS** Telephone No. (02) 6283 2677

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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1 (b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

☐ the international application as originally filed/furnished

☐ the description:

pages as originally filed/furnished
pages* received by this Authority on with the letter of
pages* received by this Authority on with the letter of

☐ the claims:

pages as originally filed/furnished
pages* as amended (together with any statement) under Article 19
pages* received by this Authority on with the letter of
pages* received by this Authority on with the letter of

☐ the drawings:

pages as originally filed/furnished
pages* received by this Authority on with the letter of
pages* received by this Authority on with the letter of

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages
☐ the claims, Nos.
☐ the drawings, sheets/figs
☐ the sequence listing (*specify*):
☐ any table(s) related to the sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages
☐ the claims, Nos.
☐ the drawings, sheets/figs
☐ the sequence listing (*specify*):
☐ any table(s) related to the sequence listing (*specify*):

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos: **1 to 12**

because:

☐ the said international application, or the said claims Nos.
relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos.
are so unclear that no meaningful opinion could be formed *(specify)*:

☒ the claims, or said claims Nos. **1 to 12**
are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claim Nos. **1 to 12**

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished
☐ does not comply with the standard

the computer readable form ☐ has not been furnished
☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	13, 14, 15	YES
	Claims	16, 17	NO
Inventive step (IS)	Claims	-	YES
	Claims	13 to 17	NO
Industrial applicability (IA)	Claims	1 to 17	YES
	Claims	-	NO

2. Citations and explanations (Rule 70.7)

The present invention relates to genetically altered animals that express altered levels of SOCS3 protein, and the use of these animals in the *in vivo* study of G-CSF induced cellular responses. In particular, the animal is a conditional mutant that expresses an altered amount of SOCS3 in cells of hematopoietic and endothelial lineages. Compounds that modulate G-CSF induced cellular responses via a SOCS molecule are also claimed.

The following documents cited in the International Search Report were considered for the basis of this report:

D1 Matsumoto et al (2003) J. Exp. Med. Vol 197(4): 425-436

D2 Croker et al (2003) Nature Immunology. Vol 4(6): 540-545

D3 Georgiades et al (2002) Genesis. Vol 34: 251-256

D4 Hörtner et al (2002) The Journal of Immunology. Vol 169: 1219-1227

D5 Hermans et al (2003) Blood. Vol 101(7): 2584-2590

D6 Croker et al (2004) Immunity. Vol 20: 153-165

D7 Kimura et al (2004) The Journal of Biological Chemistry. Vol 279(8): 6905-6910

D8 van de Geijn et al (2004) Journal of Leukocyte Biology. Vol 76: 237-244

D9 van de Geijn et al (2004) Blood. Vol 104(3): 667-674

Novelty

The invention as defined in the claims is entitled to a priority date of 4 June 2003, therefore D6 to D9 can not be considered to be part of the prior art base for the consideration of the novelty and inventiveness of the claims.

D1 discloses transgenic mice expressing a myc-tagged SOCS3 transgene. Expression from the transgene is stated to be equivalent to 5 to10 times that of endogenous SOCS3. Consequently, D1 is prejudicial to the novelty and inventiveness of claims 16 and 17.

D2 discloses conditionally mutated mice that do not express SOCS3 in liver cells and macrophages. It is considered that the phrase 'reduced levels of SOCS-3' as recited in claim 16, encompasses the absence of SOCS3 expression. Consequently, D2 is prejudicial to the novelty and inventiveness of claims 16 and 17.

(continued in Supplemental Box)

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1 to 12 are not supported by the description. Regarding the specification as a whole, the invention appears to reside in the use of a VavCre^{+}SOCS3^{fl} mouse in an *in vivo* test system for screening for compounds or agents that perturb G-CSF physiological responses via modulation of the activity or expression of SOCS3. In contrast, the claims are drawn to a disproportionately large number of possible compounds that are defined by the characteristic of modulating SOCS3. Such compounds do not owe there existence to the methods of the invention and therefore do not form part of the invention supported by the description.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: V

D3 discloses VavCre transgenic mice and the usefulness of these lines to target gene inactivation to hematopoietic and endothelial cell lineages. The document does not teach or suggest mice with reduced expression of SOCS3 and therefore does not impact on the novelty of any of the claims. However, it is considered that claims 16 and 17 are not inventive in light of the teachings of D3, when combined with the teachings of D2.

D4 teaches that in neutrophils, SOCS3 is induced by G-CSF and that SOCS3 inhibits G-CSFR mediated signal transduction. D4 does not impact on the novelty of any of the claims.

D5 teaches that in myeloid progenitor cells, SOCS3 inhibits G-CSF responses via Tyr729 of G-CSF-R. D5 does not impact on the novelty of any of the claims.

Inventive Step

Claims 13 to 15 do not involve an inventive step in light of the teachings of either D4 or D5. Each document teaches that SOCS3 is a negative regulator of G-CSF signalling. Therefore the skilled person would readily appreciate that the administration of compounds that either directly or indirectly modulate the activity or expression of SOCS3 would perturb G-CSF induced cellular responses in a mammal. Therefore the methods of claims 13 to 15 represent obvious and non-inventive applications of the teachings of D4 or D5.

Claims 16 and 17, in so far as they relate to the VavCre^{+}SOCS3$^{-/fl}$ mouse disclosed in the present application, do not involve an inventive step in light of D3 in view of D2. D2 discloses genetically altered mice that do not express SOCS3 in the liver or in macrophages. The authors also suggest that mice in which SOCS3 is not expressed in other tissues would be a valuable tool for the study of the effects of SOCS3 on signalling by cytokines. Given it is known that the VavCre mouse inactivates lox flanked genes, it would be obvious to the skilled person that a VavCre^{+}SOCS3$^{-/fl}$ mouse could be generated using the VavCre mouse disclosed in D2 and general methods in the art.